

### Amendment to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

#### Listing of Claims

1. (Currently amended) A pharmaceutical composition comprising microparticles of a polynucleotide encapsulated in a matrix comprising lipid, protein, and sugar, wherein the lipid, protein, and sugar of the matrix are not part of a substantially cross-linked polymeric shell.
2. (Currently amended) A pharmaceutical composition comprising microparticles of a polynucleotide encapsulated in a matrix, wherein the matrix comprises at least three components selected from the group consisting of lipid, protein, sugar, and synthetic polymer, wherein the components of the matrix are not part of a substantially cross-linked polymeric shell.
- 3.-6. (Canceled)
7. (Original) The pharmaceutical composition of claim 1 wherein the polynucleotide is DNA.
8. (Original) The pharmaceutical composition of claim 1 wherein the polynucleotide is RNA.
9. (Original) The pharmaceutical composition of claim 1 wherein the polynucleotide comprises RNA and DNA.
10. (Original) The pharmaceutical composition of claim 1 wherein the polynucleotide is a modified polynucleotide.

11. (Original) The pharmaceutical composition of claim 1 wherein the polynucleotide is a derivative of DNA or RNA.
12. (Original) The pharmaceutical composition of claim 1 wherein the polynucleotide is at least 100 base pairs in length.
13. (Original) The pharmaceutical composition of claim 1 wherein the polynucleotide is at least 1000 base pairs in length.
14. (Original) The pharmaceutical composition of claim 1 wherein the polynucleotide is at least 10000 base pairs in length.
15. (Original) The pharmaceutical composition of claim 1 wherein the polynucleotide is a plasmid.
16. (Original) The pharmaceutical composition of claim 1 wherein the polynucleotide encodes a pharmaceutically active protein.
17. (Original) The pharmaceutical composition of claim 1 wherein the polynucleotide encodes an immunologically active protein.
18. (Original) The pharmaceutical composition of claim 1 wherein the polynucleotide encodes a bacterial protein antigen.
19. (Original) The pharmaceutical composition of claim 1 wherein the polynucleotide encodes a viral protein antigen.
20. (Original) The pharmaceutical composition of claim 1 wherein the lipid is a naturally occurring lipid.

21. (Original) The pharmaceutical composition of claim 1 wherein the lipid is an emulsifier.
22. (Original) The pharmaceutical composition of claim 1 wherein the lipid is a surfactant.
23. (Original) The pharmaceutical composition of claim 1 wherein the lipid is positively charged.
24. (Original) The pharmaceutical composition of claim 1 wherein the lipid is negatively charged.
25. (Withdrawn) The pharmaceutical composition of claim 1 wherein the lipid has no charge.
26. (Original) The pharmaceutical composition of claim 1 wherein the lipid is a phosphatidylcholine.
27. (Original) The pharmaceutical composition of claim 1 wherein the lipid is dipalmitoylphosphatidylcholine (DPPC).
28. (Withdrawn) The pharmaceutical composition of claim 1 wherein the lipid is polyvinyl alcohol.
29. (Original) The pharmaceutical composition of claim 1 wherein the lipid is a phospholipid.

30. (Original) The pharmaceutical composition of claim 1 wherein the lipid is selected from the groups consisting of phosphoglycerides; phosphatidylcholines; dipalmitoyl phosphatidylcholine (DPPC); dioleoylphosphatidyl ethanolamine (DOPE); dioleyloxypropyltriethylammonium (DOTMA); dioleoylphosphatidylcholine; cholesterol; cholesterol ester; diacylglycerol; diacylglycerolsuccinate; diphosphatidyl glycerol (DPPG); hexanedecanol; fatty alcohols such as polyethylene glycol (PEG); polyoxyethylene-9-lauryl ether; a surface active fatty acid, such as palmitic acid or oleic acid; fatty acids; fatty acid amides; sorbitan trioleate (Span 85) glycocholate; surfactin; a poloxomer; a sorbitan fatty acid ester such as sorbitan trioleate; lecithin; lysolecithin; phosphatidylserine; phosphatidylinositol; sphingomyelin; phosphatidylethanolamine (cephalin); cardiolipin; phosphatidic acid; cerebrosides; dicetylphosphate; dipalmitoylphosphatidylglycerol; stearylamine; dodecylamine; hexadecyl-amine; acetyl palmitate; glycerol ricinoleate; hexadecyl sterate; isopropyl myristate; tyloxapol; poly(ethylene glycol)5000-phosphatidylethanolamine; and phospholipids.
31. (Original) The pharmaceutical composition of claim 1 wherein the lipid is a derivatized lipid.
32. (Original) The pharmaceutical composition of claim 1 wherein the protein is an albumin.
33. (Original) The pharmaceutical composition of claim 1 wherein the protein is a whole cell extract.
34. (Withdrawn) The pharmaceutical composition of claim 1 wherein the protein is an antibody.
35. (Withdrawn) The pharmaceutical composition of claim 1 wherein the protein is an enzyme.

36. (Withdrawn) The pharmaceutical composition of claim 1 wherein the protein is glucose oxidase.
37. (Original) The pharmaceutical composition of claim 1 wherein the sugar comprises a mixture of complex and simple sugars.
38. (Original) The pharmaceutical composition of claim 1 wherein the sugar is lactose.
39. (Original) The pharmaceutical composition of claim 1 wherein the sugar is cellulose.
40. (Original) The pharmaceutical composition of claim 1 wherein the sugar is a chemically modified sugar.
41. (Withdrawn) The pharmaceutical composition of claim 1 wherein the sugar is a glycosaminoglycan.
42. (Withdrawn) The pharmaceutical composition of claim 1 wherein the sugar is dextran.
43. (Withdrawn) The pharmaceutical composition of claim 1 wherein the sugar is chemically modified dextran.
44. (Withdrawn) The pharmaceutical composition of claim 1 wherein the sugar is chondroitin sulfate.
45. (Original) The pharmaceutical composition of claim 1 wherein the sugar is a derivatized sugar.
46. (Original) The pharmaceutical composition of claim 1 wherein the sugar is a chemically modified sugar.

47. (Original) The pharmaceutical composition of claim 1 wherein the sugar is selected from the group consisting of galactose, lactose, glucose, maltose, starches, cellulose and its derivatives, methyl cellulose, carboxymethyl cellulose, fructose, dextran and its derivatives, raffinose, mannitol, xylose, dextrans, glycosaminoglycans, sialic acid, chitosan, hyaluronic acid, and chondroitin sulfate.
48. (Original) The pharmaceutical composition of claim 1 wherein the ratio of lipid to protein to sugar is approximately 3:1:1.
49. (Original) The pharmaceutical composition of claim 1 wherein the lipid comprises 0-99% of the matrix by weight.
50. (Original) The pharmaceutical composition of claim 1 wherein the lipid comprises 3-99% of the matrix by weight.
51. (Original) The pharmaceutical composition of claim 1 wherein the lipid comprises 20-60% of the matrix by weight.
52. (Original) The pharmaceutical composition of claim 1 wherein the protein comprises 0-95% of the matrix by weight.
53. (Original) The pharmaceutical composition of claim 1 wherein the protein comprises 10-30% of the matrix by weight.
54. (Original) The pharmaceutical composition of claim 1 wherein the protein comprises 1-20% of the matrix by weight.

55. (Original) The pharmaceutical composition of claim 1 wherein the sugar comprises 0-60% of the matrix by weight.
56. (Original) The pharmaceutical composition of claim 1 wherein the sugar comprises 0.5%-50% of the matrix by weight.
57. (Original) The pharmaceutical composition of claim 1 wherein the sugar comprises 10-30% of the matrix by weight.
58. (Original) The pharmaceutical composition of claim 1 wherein the microparticles are less than 50 micrometers in diameter.
59. (Original) The pharmaceutical composition of claim 1 wherein the microparticles are less than 10 micrometers in diameter.
60. (Original) The pharmaceutical composition of claim 1 wherein the microparticles are less than 5 micrometers in diameter.
61. (Original) The pharmaceutical composition of claim 1 wherein the microparticles are less than 1 micrometer in diameter.
62. (Original) The pharmaceutical composition of claim 1 wherein the microparticles are less than 500 nanometers in diameter.
63. (Original) A method of preparing microparticles comprising a polynucleotide encapsulated in a lipid-protein-sugar matrix, the method comprising steps of:  
providing a polynucleotide;  
contacting the polynucleotide with a lipid, a protein, and a sugar; and

spray drying mixture of the polynucleotide, the lipid, the protein, and the sugar to make microparticles.

64. (Canceled)

65. (Currently amended) A method of administering an agent, the method comprising steps of:

providing a patient;

providing microparticles of a polynucleotide encapsulated in a lipid-protein-sugar matrix, wherein the lipid, protein, and sugar of the matrix are not part of a substantially cross-linked polymeric shell; and

administering the microparticles to the patient.

66. (Original) The method of claim 65 wherein the step of administering comprises injecting the microparticles into the patient.

67. (Original) The method of claim 65 wherein the step of administering comprises placing the microparticles in a body cavity of the patient.

68. (Original) The method of claim 65 wherein the step of administering comprises inhaling the microparticles.

69. (Currently amended) A method of transfecting cells, the method comprising steps of:  
providing at least one cell;  
providing lipid-protein-sugar particles containing a polynucleotide, wherein the lipid, protein, and sugar of the matrix are not part of a substantially cross-linked polymeric shell; and  
contacting the cell with the particles.

70. (Original) The method of claim 69 wherein the cells are *in vitro*.



71. (Original) The method of claim 69 wherein the cells are hematopoietic stem cells.
72. (Original) The method of claim 69 wherein the cells are embryonic stem cells.
73. (Currently amended) A method of immunizing an individual, the method comprising steps of:
- providing an individual;
  - providing microparticles comprising a polynucleotide encapsulated in a lipid-protein-sugar matrix, wherein the lipid, protein, and sugar of the matrix are not part of a substantially cross-linked polymeric shell; and
  - delivering an effective amount of the microparticles to the individual to stimulate an immune response.
74. (Original) The method of claim 73 wherein the polynucleotide encodes a protein antigen.
75. (Original) The method of claim 74 wherein the protein antigen is derived from bacteria, viruses, protozoa, or parasites.
76. (Original) The method of claim 73 wherein the microparticles further comprise an adjuvant.
77. (Original) The method of claim 73 wherein the microparticles are less than 5 micrometers in diameter.
78. (Original) The method of claim 73 wherein the microparticles are at least 5 micrometers in diameter.

79. (New) A pharmaceutical composition comprising microparticles of a polynucleotide encapsulated in a matrix comprising dipalmitoylphosphatidylcholine (DPPC), lactose, and albumin.